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~~equi infection, such that vaccinated horses demonstrate significant differences in mortality,~~
~~total clinical score, disease incidence and leukocytosis following *Streptococcus equi* challenge~~
~~as compared to non-vaccinated horses.~~

In claims 5, 9, 11, 16 and 18, line 2 in each, after the phrase "strain 709-27"
please insert --(ATCC 53186)--.

In claims 19-21, line 2 in each, please delete "CFU" and insert --Colony
Forming Unit (CFU)--.

REMARKS

Claims 1-21 are under consideration in this application. Claims 19-21 stand
objected to for informalities. Claims 1, 2, 5, 10, 15, 17 and 19-21 stand rejected under 35
U.S.C. 102(b). Claims 1, 3, 10, 17, and 19-21 stand rejected under 35 U.S.C. 102(a).
Claims 1-21 stand rejected under 35 U.S.C. 103(a). The specification and claims 1, 5, 9, 11,
16, 18 and 19-21 are amended. Support for the amendment of claim 1 is found in the
specification at page 9, lines 8 and 13-16. Support for the amendment of claims 5, 9, 11, 16
and 18 is found in the specification at page 5, line 8.

Reconsideration of this application is respectfully requested.

THE SPECIFICATION AND STRAIN DEPOSIT INFORMATION

The Examiner states that the specification lacks complete information for the
deposit of *Streptococcus equi* (*S. equi*) strain 709-27. The Examiner states that it is not clear
that the use of the live attenuated strain 709-27 is known and publicly available. Applicants
submit that this strain is fully identified in the specification at page 5, line 8. Applicant notes

that said strain is publicly available as ATCC Strain number 53186 and has been since 1993.

This is evidenced by the copy of the ATCC strain information attached hereto as Exhibit A.

Claims 5, 9, 11, 16 and 18 have been amended to add this ATCC strain identification number information.

OBJECTIONS TO THE CLAIMS

Claims 19-21 are objected to because of the use of the abbreviation "CFU".

Applicant submits that the abbreviation CFU is well known in the art and need not be replaced, however, in the interest of expediting prosecution, applicant has amended the specification and claims 19-21 to insert the non-abbreviated phrase "Colony Forming Unit" before "CFU". CFU is defined as Colony Forming Unit in the copy of an excerpt from Stedman's Medical Dictionary which is provided herewith as Exhibit B. As the phrase CFU is both well known and well used in the art, applicant submits that no new matter is being added.

In light of the foregoing, withdrawal of the objection of claims 19-21 is respectfully requested.

REJECTIONS UNDER 35 U.S.C. § 102(b)

Claims 1, 2, 5, 10, 15, 17 and 19-21 stand rejected under 35 U.S.C. 102(b) as being anticipated by either Timoney (U.S. Patent No. 5,183,659) ("'659 patent") or Timoney (PCT WO 87/00436) ("'436 PCT"). The Examiner contends that the Timoney references each disclose a vaccine composition comprising a live attenuated and non-encapsulated *S. equi* strain 709-27 (ATCC 53186) and an immunostimulant, i.e. an M protein

fragment which stimulates an immunological response in the nasopharyngeal mucosa of an equine. Applicant respectfully traverses the rejection.

Claim 1 recites a composition comprising a live attenuated *Streptococcus equi* and an immunostimulant having the property of stimulating mucosal immunity. Applicant notes that the M protein of the Timoney references is part of the *S. equi* bacterial strain 709-27 and is not an additional immunostimulant added to enhance the immunogenicity of the vaccine as claimed herein. Indeed, Timoney states that the:

"vaccine comprises an avirulent strain of *S. equi* formed by mutating a virulent strangles causing *S. equi* strain to render it avirulent while retaining thereon protein which provides an acid extract M protein fragment"

See '659 patent at col.2, lines 56-60 and '436 PCT at page 4, lines 19-23, emphasis added.

The Timoney vaccine thus solely discloses an attenuated *Streptococcus equi* that has and retains the M protein on it, such that said *Streptococcus equi* provides a 41K M protein fragment following acid extraction. See '659 patent at col. 2, lines 59-61; col. 3, lines 3-4; col. 6, line58-col. 7, line 8. The M protein is "retained on" the *Streptococcus equi*, i.e., is a part of it, and is not a separate immunostimulant. Nowhere do the Timoney references provide for an immunostimulant to be administered in addition to the attenuated *Streptococcus equi* which has the M protein on it. The cited references clearly do not disclose the limitations of the recited claims.

In light of the foregoing, applicant respectfully requests reconsideration and withdrawal of the rejection of claim 1 under 35 U.S.C. 102(b). In addition, since claims 2, 5, 10, 15, 17 and 19-21 contain all of the limitations, features and attributes of claim 1, these

claims should also be found non-obvious over the cited art. In re Fine, 5 U.S.P.Q. 2d 1596, 1600 (Fed. Cir. 1988).

REJECTIONS UNDER 35 U.S.C. § 102(a)

Claims 1, 3, 10, 17 and 19-21 stand rejected under 35 U.S.C. 102(a) as being anticipated by Hartford et al (European Patent Application No. EP 0 786 518 A1) ("Hartford"). Applicant respectfully traverses the rejection.

Claim 1 has been amended to recite a vaccine composition that elicits protective immunity from *Streptococcus equi* infection such that vaccinated horses demonstrate significant differences in mortality, total clinical score, disease incidence and leukocytosis following *Streptococcus equi* challenge as compared to non-vaccinated horses.

Hartford teaches a new mutated *Streptococcus equi* strain TW 928, which comprises a large deletion (about 1 kb) in its genome. Hartford nowhere exemplifies the use of adjuvans in its vaccine. Importantly, Hartford fails to demonstrate administration of its vaccine to horses and fails to demonstrate that its vaccine elicits protective immunity in horses. In other words, Hartford nowhere teaches that its vaccine provides protection against a *Streptococcus equi* challenge in horses. Indeed, with regard to the challenge and testing of an efficacious vaccine, Hartford solely discloses administration of its *Streptococcus equi* strain to BALB/c mice. The only tests in horses were carried out to determine the safety of the attenuated virus. No vaccination and challenge with live virus was ever carried out in horses. See Example V at page 12.

The Hartford study cannot demonstrate an efficacious horse vaccine because no such demonstration in horses was ever performed. Hartford thus does not teach an efficacious *Streptococcus equi* horse vaccine (either alone, or in combination with other viral components) formed from live attenuated viruses in conjunction with an immunostimulant such that vaccinated horses demonstrate significant differences in mortality, total clinical score, disease incidence and leukocytosis following *Streptococcus equi* challenge as compared to non-vaccinated horses. The cited reference does not disclose the limitations of the recited claims.

In light of the foregoing, applicant respectfully requests reconsideration and withdrawal of the rejection of claim 1 under 35 U.S.C. 102(a). In addition, since claims 3, 10, 17 and 19-21 contain all of the limitations, features and attributes of claim 1, these claims should also be found non-obvious over the cited art. In re Fine, 5 U.S.P.Q. 2d 1596, 1600 (Fed. Cir. 1988).

REJECTIONS UNDER 35 U.S.C. § 103(a)

Claims 1-21 are rejected under 35 U.S.C. 103(a) over Timoney or Timoney in view of Hartford and Gerber (U.S. Patent No. 4,806,350) ("Gerber"). Applicant respectfully traverses the rejection.

The Examiner relies on the Timoney references in combination with Hartford and Gerber in support of an obviousness rejection of claims 1-21. All of claims 2-21 incorporate the limitations of claim 1. The Examiner bears the burden of establishing a *prima facie* case of obviousness based upon the art. Both the suggestion of making the present invention and the expectation of success must be founded in the prior art, not in applicants'

disclosure. In re Dow Chemical Co., 5 U.S.P.Q.2d 1529, 1531 (Fed. Cir. 1988.) Applicant respectfully submits that neither of these criterion have been met. An analysis of a combination of Timoney or Timoney in view of Hartford and Gerber demonstrates that there is neither a suggestion nor motivation to make the efficacious horse vaccines of the invention comprising a live attenuated *Streptococcus equi* and an immunostimulant, said immunostimulant having the property of stimulating mucosal immunity, wherein said vaccine elicits protective immunity from *Streptococcus equi* infection in horses, such that vaccinated horses demonstrate significant differences in 1) mortality, 2) total clinical score, 3) disease incidence and 4) leukocytosis following *Streptococcus equi* challenge as compared to non-vaccinated horses.

With regard to the Timoney references, as discussed above, the references do not apply to the invention as claimed. The Timoney M protein is "retained on" the *Streptococcus equi*. In other words, the M protein is a part of the *S. equi* bacterium and is not a separate immunostimulant. Nowhere do the Timoney references provide for an immunostimulant to be administered in addition to the attenuated *Streptococcus equi*.

With regard to the Hartford reference, as discussed above, the presently claimed invention encompasses a *Streptococcus equi* vaccine that includes an immunostimulant having the property of stimulating mucosal immunity which elicits protective immunity from *Streptococcus equi* infection such that vaccinated horses demonstrate significant differences in mortality, total clinical score, disease incidence and leukocytosis following *Streptococcus equi* challenge as compared to non-vaccinated horses. The Hartford study cannot be relied upon to

demonstrate the efficacy of a horse *Streptococcus equi* vaccine because Hartford never tests the efficacy of its vaccine in horses. A person of ordinary skill in the art would not expect to enhance the protective immunity of a vaccine in an animal if that vaccine had not been shown to be protective that animal. Indeed, no one reading the mouse study of Hartford would have a reasonable expectation that administration of the Hartford vaccines would provide protective immunity in horses, let alone demonstrate significant differences in mortality, total clinical score, disease incidence and leukocytosis following *Streptococcus equi* challenge as compared to non-vaccinated horses.

With regard to Gerber, while the reference does teach the use of saponin as an adjuvant, nowhere does it motivate the reader to use it as an immunostimulant for stimulating mucosal immunity as claimed herein.

There is no motivation to combine the references and there is no motivation or suggestion in the combination of references to make the present invention. Applicant submits that the Examiner has relied on hindsight to arrive at the determination of obviousness. The combination of references do not suggest that the attenuated viruses of Timoney or Hartford used in combination with an immunostimulant for mucosal immunization would, upon administration to and challenge in horses, provide the required protective immunity encompassing a decrease in mortality, total clinical score, disease incidence and leukocytosis as claimed. Gerber nowhere makes up for the deficiencies of Timoney or Hartford.

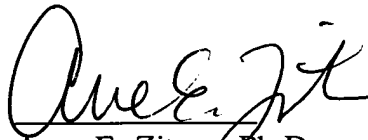
In light of the foregoing, Applicant respectfully requests reconsideration and withdrawal of the rejection of claim 1 under 35 U.S.C. 103(a). In addition, since claims 2-21

each contain all of the limitations, features and attributes of claim 1, these claims should also be found non-obvious over the cited art. In re Fine, 5 U.S.P.Q. 2d 1596, 1600 (Fed. Cir. 1988).

CONCLUSION

In light of the foregoing, reconsideration and withdrawal of all of the objections and rejections are respectfully requested. Applicant submits that all of claims 1-21 are in condition for allowance. Prompt and favorable allowance of the claims is requested. If for any reason the Examiner concludes that any of the claims as amended is not properly allowable, the Examiner is respectfully requested to contact the undersigned by telephone at 212-527-7679.

Respectfully submitted,



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Amendment
Serial No.: 09/007,385